REMARKS/ARGUMENTS

In response to the Office Action of April 22, 2003, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim 1 has been amended. Claims 2-38 have been canceled. Claims 39-46 have been added. Claims 1 and 39-46 are pending in the instant application.

No new matter has been added by the amendments to the specification.

Several protocols in the experimental section of the detailed description have been amended to properly identify the trademark SEPHAROSE.

No new matter has been added by the addition of new claims 39-46. New claims 39-46 correspond with cancelled claims 2-38. The above additions to the claims find basis in the original disclosure at page 25, line 16 to page 26, line 22. The method of new claim 39 is described in detail at pages 37-47. Page 47, lines 19-23 refers to use of various types of samples and page 38, line 20 to page 39, line 10 refers to different mass spectrometric techniques. Page 46, line 19 refers to practicing the claimed methods with a human patient. Pages 47-48 describe kits contemplated for use with the claimed methods. Lines 17-19 on page 47 refer particularly to the immobilizing on solid supports and labeling of components of the contemplated kits. It is clear from these specific recitations

and from the description of methods utilized that the methods and types of kits recited in the newly added claims (39-46) were fully contemplated by the inventors at the time of filing and were enabled by virtue of the disclosure as originally filed.

Restriction/Election

Applicants herein affirm the election of Group I (claims 1, 2 and 10-28) without traverse for prosecution on the merits. The election was made during a telephone conference with the Examiner on January 15, 2003.

This application is related in claim format to several pending applications of which serial number 09/846,352 is exemplary. The biopolymer marker of serial number 09/846,352 was found to be novel and subsequently claims reading on methods and kits limited to its use were rejoined with the claims reading on the biopolymer marker under *Ochai*. In an effort to maintain equivalent scope in all of these applications, Applicants respectfully request that the Examiner reconsider the restriction requirement in the instant application to include the new claims (39-46) added herein by amendment. If the peptides of SEQ ID NOS:1 and 2 are found to be novel as diagnostic for insulin resistance, methods and kits limited to their use as markers diagnostic for insulin resistance should also be found novel.

Rejections under 35 USC 112 (second paragraph)

Claims 1, 2 and 10-28, as originally presented, stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that claims 1, 10, 18 and 28 are vague and confusing in reciting the phrase " at least one analyte thereof" because it is unclear how a material can be an analyte of a biopolymer marker. Claim 1 has been amended and does recite the phrase "at least one analyte thereof". Claims 10, 18 and 28 have been canceled and the phrase "analyte thereof" is not recited in any of the remaining pending claims.

The Examiner alleges that it is unclear what is being claimed in claim 1, SEQ ID NO:1 or SEQ ID NO:2 or any analyte thereof. Claim 1 has been amended to clearly claim a biopolymer marker peptide selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2. The phrase "analyte thereof" is not recited in the amended claim 1 or any of the other remaining pending claims.

The Examiner alleges that claims 12 and 14 are vague and indefinite in relation to claim 10 in reciting "at least one labeled biochemical material" because it is unclear as to whether the biochemical material in claims 12 and 14 is the same as the biochemical material recited in claim 10, but including a label. Claims 12 and 14 have been canceled and the phrase "at least one

labeled biochemical material" is not recited in any of the remaining pending claims.

The Examiner alleges that claims 15, 23, 24 and 26-28 lack positive limitations. Claims 15, 23, 24 and 26-28 have been cancelled thus rendering this rejection moot.

The Examiner alleges that the term "therefore" in claims 17 and 25 should be --thereof--. Claims 17 and 25 have been canceled and neither "therefore" nor --thereof-- is recited in any of the remaining pending claims.

Accordingly, applicants have now clarified the metes and bounds of the claims and respectfully request that all of the above-discussed rejections under 35 U.S.C. 112, second paragraph be withdrawn.

Rejection under 35 USC 102(b)

Claims 1 and 2, as originally presented, stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Durham *et al.* (US Patent Application Publication; US 2002/0164668 A1, published on November 7, 2002).

The Examiner alleges that Durham *et al.* teach using various AD markers comprising the recited SEQ ID NO:1 (see Table IV, AF-22). Durham *et al.* also teach using the markers for screening and diagnosis of AD disease. The Examiner also alleges that claim 2 is an improper dependent claim and the intended use is not given

patentable weight.

It is noted that the filing date of the instant application is November 21, 2001 and the publication date of Durham *et al.* is November 7, 2002. US patent application publications are prior art under 35 U.S.C. 102(b) as of the publication date (see MPEP 901.03). 35 U.S.C. 102(b) reads: A person shall be entitled to a patent unless (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, **more than one year prior** to the date of application for patent in the United States. Durham *et al.* was not publically available more than one year prior to applicants' filing date, thus the Durham *et al.* reference is not properly applied under 35 U.S.C. 102(b). However, the rejection will be responded to as if it was properly applied.

Claim 2 has been cancelled, thus rendering the rejection of claim 2 moot. Claim 1 has been amended to clearly claim a biopolymer marker peptide selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 diagnostic for insulin resistance.

Original claim 2 read: The biopolymer marker of claim 1 wherein said disease state is predictive of Alzheimers disease. However, insulin resistance is the disease state wherein said biopolymer markers of claim 1 are predictive. This is evidenced at page 46, lines 4-10 of the original disclosure. Claim 2 was amended to recite "insulin resistance" in place of "Alzheimers disease" in

the Supplemental Preliminary Amendment filed on April 29, 2002.

Durham *et al.* disclose methods and compositions for screening, diagnosis and treatment of Alzheimers disease and for screening and development of drugs for treatment of Alzheimers disease (see Summary of Invention, page 1 of Durham *et al.*). While Durham *et al.* do disclose SEQ ID NO:1 of the instant invention at Table IV-AF-22; Durham *et al.* do not disclose this sequence as diagnostic for insulin resistance. Nor does Durham *et al.* teach any methods, compositions or kits useful for screening, diagnosis and treatment of insulin resistance. SEQ ID NO:1 as claimed in the instant invention is diagnostic for insulin resistance, thus Durham *et al.* do not anticipate claim 1 as amended herein.

Accordingly, Applicants respectfully submit that the claims, as instantly presented, now distinguish over the compositions taught by Durham *et al.* and respectfully request that this rejection be withdrawn.

Rejection under 35 USC 103(a)

Claims 1, 2 and 10-28, as originally presented, stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Durham *et al.* (US Patent Application Publication; US 2002/0164668 A1, published on November 7, 2002) in view of Hutchens *et al.* (US 6,225,047 B1).

The Examiner asserts that it would have been obvious to one

of ordinary skill in the art at the time that the instant invention was made to make a diagnostic assay kit in combination of the teaching of Durham *et al.*, *i.e.* SEQ ID NO:1 which comprises a biopolymer used as a diagnostic marker of a disease state, *e.g.* Alzheimers disease, with the method of Hutchens *et al.* which uses SELDI-MS for differential detection of biopolymers because using kit containing antibodies for detection of target materials is routine in the art for clinical purposes.

The remaining pending claims of the instant application are drawn to specific biopolymer peptide markers (SEQ ID NOS:1 and 2) specifically diagnostic for insulin resistance and to methods and kits using such biopolymer peptide markers.

Durham *et al.* disclose methods and compositions for screening, diagnosis and treatment of Alzheimers disease and for screening and development of drugs for treatment of Alzheimers disease (see Summary of Invention, page 1 of Durham *et al.*). While Durham *et al.* do disclose SEQ ID NO:1 of the instant invention at Table IV-AF-22; Durham *et al.* do not disclose this sequence as diagnostic for insulin resistance as does the instant invention. Nor does Durham *et al.* teach any methods, compositions or kits useful for screening, diagnosis and treatment of insulin resistance. Thus, it is established that Durham *et al.* do not disclose any biopolymer markers for insulin resistance nor does Durham *et al.* disclose any methods or kits using such markers.

Hutchens *et al.* teach a method for identifying analytes that are differentially present between two samples through the use of the techniques of retentate chromatography and desorption spectrometry. Although the instant invention also teaches a method for identifying analytes that are differentially present between two samples through the use of the techniques of chromatography and spectrometry, the chromatographic methods of the instant invention are distinct from retentate chromatography. Page 45, line 4 of the instant specification refers to the use of micro-chromatographic columns which evidences the use of a form of chromatography known as partition chromatography. Partition chromatography and retentate chromatography are not identical methods. Retentate chromatography is limited by the fact that if unfractionated body fluids (blood, blood products, saliva, urine, cerebrospinal fluid and lymph) along with tissue samples, are applied to the adsorbent surfaces, the biopolymers present in the greatest abundance will compete for all the available binding sites and thereby prevent or preclude less abundant biopolymers from interacting with them, thereby reducing or eliminating the diversity of biopolymers which are readily ascertainable (see the instant specification at pages 24 and 25). The instant invention is characterized by the use of a combination of preparatory steps (chromatography and 1-D tricine polyacrylamide gel electrophoresis) that maximizes the diversity of biopolymers discernable from a sample thus overcoming the limitation of the

retentate chromatography method as taught by Hutchens *et al.* Furthermore, Hutchens *et al.* do not suggest alternative means for the identification of differentially present analytes nor do they suggest preparatory steps to overcome the limitations of retentate chromatography. Thus, even if Durham *et al.* did disclose biopolymer markers diagnostic for insulin resistance and one of ordinary skill in the art identified such markers through use of the methods as taught by Hutchens *et al.*, one of ordinary skill in the art would not have arrived at the instant invention.

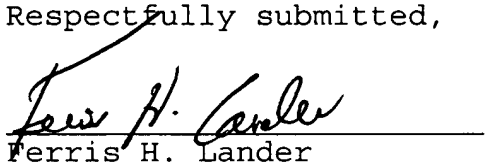
There are no teachings or suggestions in either reference (Durham *et al.* and Hutchens *et al.*) which would motivate one of ordinary skill in the art to use preparatory steps in combination with methods of chromatography and spectrometry to identify any biopolymer markers diagnostic for insulin resistance.

Thus, it is respectfully submitted that the combination of Durham *et al.* in view of Hutchens *et al.* fails to reasonably teach or suggest to one of ordinary skill in the art the elements of the invention as specifically set forth in the instantly amended claims.

CONCLUSION

In light of the foregoing remarks and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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